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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/815,119	WEN ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-25,27 and 28* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22, 23 and 25, 27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of request for continued examination under 37 CFR 1.114 and remarks filed 02/05/09. No claim 26 is amended. Claims 22-25, 27 and 28 are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/05/09 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 22, 23, 25, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter.

4. Claim 22 requires the application of the semisolid compositions to produce increased blood flow through the region within thirty minutes. This particular effect due to the

administration of the composition does not appear to have support from the specification as originally filed.

Response to Arguments

5. Applicant's arguments filed 02/05/09 have been fully considered but they are not persuasive.

6. Applicant has indicated that page 35, Table 3, Fig. 3, page 37, lines 1-9 (Table 4), page 6, lines 24, 25 corresponding to paragraph [0019] of the published application, page 40 (Table 6), Fig. 4, page 44 (Table 9), Example 4, Fig. 6, Example 5 including page 47, page 45, lines 16-22, Table 11 and page 48, line 21 to page 49 line 3, all provide support for the limitation that application of the semi-solid composition produces increase in blood flow through the region of vasospasm within 30 minutes of the application. The examiner disagrees. The closest to the limitation is at 6, lines 24-26 where it is stated that the vascular perfusion volume to the tissue returns to normal within 30 minutes …after application of the composition.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 22, 23, 25, 27and 28 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Buyuktimkin et al. (US 6,046,244).

9. Claim 22 is a method of treating vasospasm; the method topically applies a semisolid composition to a region of the subject's tissue requiring treatment of vasospasm; the application of the composition produces an increase in blood flow through the region of vasospasm within 30 minutes of application. The composition that is topically applied to the region of the subjects tissue comprises vasoactive prostaglandin, penetration enhancer, polymeric thickener, lipohilic component, buffer system that buffers the composition at pH of about 3 to about 7.4. Claim 22 does not limit or recite the amount the prostaglandin or recite what amount of the semi solid composition is effective in treating vasospasm. Rather, giving the claims their broadest reasonable interpretation, the claims teach that the treatment of vasospasm derives from the resultant effect of topical application of the semi solid composition containing prostaglandin in any amount. Further, the "wherein" clause in the last two sentences of claim 22 expresses the intended result of the application of the semi-solid composition to skin tissue.

10. The ART:

11. Buyuktimkin provides a semi solid, separation resistant composition that provides relatively rapid sustained delivery of prostaglandin E_1 (column 2, lines 5 and 6) when the composition is topically applied to the target tissue of a patient (column 8, lines 11-19) with the composition contemplated to treat perivascular disease, male impotency and other disorders treated by prostaglandin E_1 (column 8, lines 6-9). In the background, Buyuktimkin discloses that "prostaglandin E1 is a vasodilator useful to maintain open blood vessels and therefore, to treat peripheral vascular disease among other ailments" (column 1, lines 27-29).

12. The composition of Buyuktimkin comprises prostaglandin E_1, polysaccharide gum, lipophilic compound, penetration enhancer and buffer system that is capable of buffering the

composition at a pH of about 3 to about 7.4 (abstract; column 2, lines 9-28) so that the composition of Buyuktimkin meets the composition that is claimed to be applied to a subject's skin in claim 22. The prostaglandin E_1 meets the limitation of the prostaglandin of claims 22 and 25. The penetration enhancer of Buyuktimkin is substituted alkanoate such as dodecyl 2-(N,N dimethylamino)-propionate (DDAIP) (column 3, lines 5-54) meeting the penetration enhancer of claims 22 and 27. The polysaccharide gum of Buyuktimkin is galactomannan, which includes guar gum and locust bean gum (column 5, lines 46-49) meeting guar gum polymer thickener of claim 22. The lipophilic component in the composition of Buyuktimkin is aliphatic C_1-C_8 alcohol or aliphatic C_8-C_{30} ester (abstract; column 2, lines 15-17; column 6, lines 28-31) meeting claimed lipophilic component of claims 22 and 28. Buyuktimkin contemplates applying the composition to the skin of a patient (column 8, lines 11-13) so that the limitation of topical application to a subject's tissue as in claim 22 and where the tissue is skin as in claim 23 is met.

13. For the wherein clause in the last two lines of claim 22, "the application of the semi-solid composition produces an increase in blood flow through the region of vasospasm within thirty minutes of the application" expresses the intended result of the application of the semi-solid composition to skin tissue so that the application of the same composition by Buyuktimkin would result or induce the intended result from the application of the composition where the process step of application is positively recited.

14. One of the goals of Buyuktimkin is to keep blood vessels open which inherently meets the goal of treating narrowing of blood vessels or vasospasm so that although, Buyuktimkin does not use the term vasospasm, application of the same composition as is applied by instant claim

22 would inherently treat vasospasm as it keeps blood vessels open. Thus, the claims are anticipated by Buyuktimkin.

15. In the alternate, it is known in the art that prostaglandin E_1 is a vasodilator and potent inhibitor of platelet aggregation and is used to treat vasospastic disease as evidenced in the background of Buyuktimkin and also by Clifford in the "Treatment of vasospastic disease with prostaglandin E1," in Br Med J. 1980 October 18; 281(6247): 1031–1034 (see the whole document with emphasis in the section on Summary and Conslusions).

16. Therefore, taken the teaching of Buyuktimkin, one having ordinary skill in the art at the time the invention was made would reasonably expect that topically applying a semi-solid composition containing prostaglandin E_1, polysaccharide gum, lipophilic compound, penetration enhancer and buffer system that is capable of buffering the composition at a pH of about 3 to about 7.4 (abstract; column 2, lines 9-28) to a patient's skin would keep blood vessels open as a vasodilator according to the background disclosure of Buyuktimkin and to provide prolonged treatment of peripheral vascular disease and other diseases treated with prostaglandin E1 (see column 1, lines 27-29; column 8, lines 6-8) or would treat vasospastic disease in view of the evidence provided by Clifford. With regards to the rejection in the alternative, the applicant bears the burden of showing that the composition of Buyuktimkin containing prostaglandin E_1 would not keep blood vessels open or treat narrowing of blood vessels or treat vasospasm. "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Response to Arguments

17. Applicant's arguments filed 02/05/09 have been fully considered but they are not persuasive. Applicant traverses the rejections for the following.

18. a) Buyuktimkin reference does not contain the word vasospasm; that Buyuktimkin is silent on the issue of whether the disclosed composition would have an effect on blood vessel diameter within 30 minutes of being applied to tissue; that the working examples use shed snake skin; that there is no disclosure in the amount of prostaglandin E_1 that might be transported across the snake skin at time points earlier than one hour; that there is no disclosure or suggestion of how the in vitro result would translate to living subject as to whether an effective amount of prostaglandin E_1 might be transported across living skin into the underlying vasculature; that the court reversed an inherency rejection that was based on what would result from optimization of conditions and not what was necessarily present in the prior art in the *in re Rijckaert* decision; that the Examiner presented no evidence or scientific reasoning that the Buyuktimkin reference meets the limitations of the claims.

19. The examiner disagrees that the anticipatory rejection under 35 USC 102 by Buyuktimkin should be withdrawn as argued by applicant in a) above. While Buyuktimkin does not use the term vasospasm, Buyuktimkin specifically teaches the composition used in the claims to treat vasospasm by topical application to a tissue such as the skin (claims 22 and 23), Buyuktimkin applies the same composition to the skin of a patient and in the background teaches that "prostaglandin E1 is a vasodilator useful to maintain open blood vessels and therefore, to treat peripheral vascular disease among other ailments" (column 1, lines 27-29). It is also known in the art that prostaglandin E_1 is a vasodilator and potent inhibitor of platelet aggregation and is

used to treat vasospastic disease as evidenced by Clifford. Furthermore, Buyuktimkin teaches that the composition treats peripheral vascular disease and vasospastic disease is a peripheral vascular disease as evidenced by lines 4 and 5 of column 2 of US 4,311,707 to Birnbaum et al. Therefore, the background of Buyuktimkin and other prior art such as Clifford and Birnbaum is the examiner's reasoning supporting the position that the composition containing prostaglandin E_1 would inherently produce the same effect of treating vasospasm when the composition is applied to the skin. Furthermore, with regards to the effect on blood vessel within 30 minutes of application of the composition, it is noted that the wherein clause expresses the intended result of the application of the semi-solid composition to skin tissue since the process step is positively recited as applying the composition to tissue. The claims do not recite effects on the dfiameter of the blood vessel. For applicant's statement that the working example uses shed snake skin, it is noted that a prior art reference such as Buyuktimkin is not limited to the working examples and the disclosure is clear that the composition is topically applied to the skin of a patient. Regarding the lack of disclosure of the amount of prostaglandin E_1 by Buyuktimkin, it is noted that the claims do not recite amounts of prostaglandin E_1. For the transportation of prostaglandin E_1 contained in composition of Buyuktimkin across living tissue, it is noted that prostaglandin E_1 is a known compound and its effect is also known and Buyuktimkin teaches applying the composition comprising penetration enhancers to skin of patient. With respect to the *in re Rijckaert* decision, it is noted that the composition of Buyuktimkin topically applied to a patient's skin anticipates the composition applied by the instant claims to the skin so that in the present rejections, an optimization of conditions is not required.

20. b) Applicant argues that the administration of prostaglandin E_1 occurs over a period of hours to days in the Clifford reference so that the combination of Buyuktimkin and Clifford would not produce the effect of increasing blood flow through the region of vasospasm. The examiner disagrees because Buyuktimkin teaches the same method step of topical application of a composition that is the same as the composition applied in the claims and the where in clause expresses the intended result of the application of the semi-solid composition to skin tissue, the process step of application having been positively recited. Clifford is an evidentiary reference showing that prostaglandin E_1 is effective to treat vasospastic disease.

21. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Examiner, Art Unit 1618